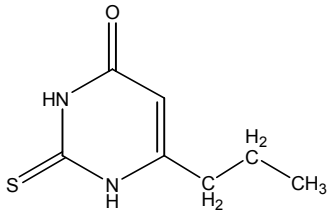
PROPYLTHIOURACIL
CAS No. 51-52-5
First Listed in the *Fourth Annual Report on Carcinogens*



CARCINOGENICITY

Propylthiouracil is *reasonably anticipated to be a human carcinogen* based on sufficient evidence for the carcinogenicity of in experimental animals (IARC V.7, 1974; IARC S.4, 1982; IARC S.7, 1987). When administered in the diet, propylthiouracil induced chromophobe adenomas of the anterior pituitary and carcinomas of the thyroid in mice and solid and cystic type adenomas of the thyroid in female rats. Propylthiouracil administered in the drinking water induced increased incidences of thyroid carcinomas and adenomas in rats of both sexes, malignant thyroid lesions, with some metastases, in hamsters of both sexes, and thyroid adenomas in male guinea pigs. Simultaneous administration of propylthiouracil and dried thyroid powder induced single or multiple chromophobe adenomas of the pituitary and carcinomas and adenomas of the thyroid in rats of both sexes. Administration of propylthiouracil and potassium iodide in the drinking water increased the incidence of thyroid adenomas and induced one carcinoma in rats. In a short-term study, oral administration of propylthiouracil induced hyperplasia of the thyroid in dogs (IARC V.7, 1974; IARC S.4, 1982). When administered orally to rats with *N*-methyl-*N*-nitrosourea given intravenously or *N*-nitrosobis(1-hydroxypropyl)amine intraperitoneally, it induced malignant thyroid tumors (IARC S.7, 1987).

There are no data available to evaluate the carcinogenicity of propylthiouracil in humans (IARC V.7, 1974; IARC S.4, 1982; IARC S.7, 1987). In a survey of 331 hyperthyroid patients treated with antithyroid drugs and later with thyroidectomy, four malignant thyroid lesions were detected in patients diagnosed with Grave's disease, whose drug therapy had continued for at least one year. There has also been a single case report of acute myeloblastic leukemia in a woman following propylthiouracil treatment (IARC S.4, 1982; Aksoy et al., 1974).

PROPERTIES

Propylthiouracil occurs as a white, crystalline powder with a starch-like appearance and a bitter taste. It is sensitive to light and prolonged exposure to air. It is slightly soluble in water at 20^{o} C, soluble in boiling water, ethanol, acetone, and aqueous solutions of ammonia and alkali hydroxides and practically insoluble in ether, chloroform, and benzene. It is incompatible with strong oxidizers, strong acids and strong bases. It forms complexes with divalent metals. When heated to decomposition, propylthiouracil emits toxic fumes of nitrogen oxides (NO_x) and sulfur oxides (SO_x). Propylthiouracil is commercially available in the United States as a USP grade containing 98%-100.5% active ingredient on a dried basis, with small amounts of thiourea present as an impurity.

USE

Propylthiouracil is used widely as an antithyroid agent for the treatment of hyperthyroidism. Veterinary applications of propylthiouracil reportedly included its use as a metabolic depressant to promote fattening in animals, but no evidence was found to indicate that propylthiouracil presently is used for this purpose (IARC V.7, 1974).

PRODUCTION

Current production data for propylthiouracil are not available, and the USITC does not identify any producers. The Chem Sources International directory identified one U.S. supplier for 1988-1989 (Chem Sources International, 1988). The 1986 Chem Sources USA directory identified three producers and several suppliers of the compound (Chem Sources, 1986). The 1979 TSCA Inventory identified one producer of propylthiouracil producing 500 lb in 1977 and one importer with no reported import volume (TSCA, 1979). No data on exports of propylthiouracil were available.

EXPOSURE

The primary routes of potential human exposure to propylthiouracil are ingestion, inhalation, and dermal contact. The usual oral dose for the treatment of hyperthyroidism is 100 mg every 8 hr. In 5% of the cases, this dosage may be increased up to 600 mg daily, divided (IARC V.7, 1974). Potential occupational exposure to propylthiouracil may occur during the production, formulation, packaging, or administration of the pharmaceuticals. The National Occupational Hazard Survey, conducted by NIOSH from 1972 to 1974, estimated that 297 workers were potentially exposed to propylthiouracil in the workplace (NIOSH, 1976). The National Occupational Exposure Survey (1981-1983) indicated that 1,775 workers, including 817 women, potentially were exposed to propylthiouracil (NIOSH, 1984). This estimate was derived from observations of the use of the actual compound (89% of total observations) and tradename products (11%).

REGULATIONS

EPA requires handling and report/recordkeeping for propylthiouracil under the Resource Conservation and Recovery Act (RCRA). FDA regulates the use of propylthiouracil as a pharmaceutical to treat hyperthyroidism under the Food, Drug, and Cosmetic Act (FD&CA). OSHA regulates propylthiouracil under the Hazard Communication Standard and as a chemical hazard in laboratories. Regulations are summarized in Volume II, Table B-130.